P=Hetacillin content of the hetacillin working standard in percent.

(6) *Identity.* Proceed as directed in § 436.211 of this chapter, using a 1 percent potassium bromide disc prepared as directed in paragraph (b)(1) of that section.

(7) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[39 FR 18976, May 30, 1974, as amended at 42 FR 59857, Nov. 22, 1977; 44 FR 10379, Feb. 20, 1979; 50 FR 19918, May 13, 1985]

§ 440.29 Hetacillin potassium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality and purity.* Hetacillin potassium is the potassium salt of hetacillin. It occurs as a fine, white to light buff powder. It is so purified and dried that:

(i) Its potency is not less than 735 micrograms of ampicillin per milligram.

(ii) [Reserved]

(iii) Its moisture content is not more than 1.0 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 7.0 and not more than 9.0.

(v) Its hetacillin content is not less than 82 percent and not more than 95.5 percent.

(vi) It gives a positive identity test for hetacillin potassium.

(vii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5(b) of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, hetacillin content, identity, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed for ampicillin in § 436.105 of this chapter, using the ampicillin working standard as the standard of comparison and preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.1*M* potassium phosphate buffer pH 8.0 (solution 3), to give a stock solution of convenient concentration. Further dilute the stock solution with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(2) [Reserved]

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(5) *Hetacillin content.* Proceed as directed in § 440.25(b)(5), except use about 110 milligrams of sample and calculate the hetacillin content as follows:

$$\text{Percent hetacillin} = \frac{C \times 5{,}000 \times P}{\text{Weight of sample in milligrams}}$$

where:

C=Concentration in milligrams of hetacillin per milliliter of the final solution of the sample obtained from the standard response line.

P=Hetacillin content of the hetacillin working standard in percent.

(6) *Identity.* Proceed as directed in § 436.211 of this chapter, using a 1 percent potassium bromide disc prepared as directed in paragraph (b)(1) of that section.

(7) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[39 FR 18976, May 30, 1974, as amended at 42 FR 59857, Nov. 22, 1977; 44 FR 10379, Feb. 20, 1979; 50 FR 19918, May 13, 1985]

§ 440.29a Sterile hetacillin potassium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Hetacillin potassium is the potassium salt of hetacillin. It occurs as a fine, white to light buff powder. It is so purified and dried that:

(i) Its potency is not less than 735 micrograms of ampicillin per milligram. If it is packaged for dispensing, its potency is satisfactory if it contains not less than 90 percent and not more than 120 percent of the number of milligrams of ampicillin that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not more than 1.0 percent.

(vi) Its pH in an aqueous solution containing 10 milligrams per milliliter (or when reconstituted as directed in the labeling, if it is packaged for dispensing) is not less than 7.0 and not more than 9.0.

(vii) Its hetacillin content is not less than 82 percent and not more than 95.5 percent.

(viii) It gives a positive identity test for hetacillin potassium.

(ix) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, hetacillin content, identity, and crystallinity.

(ii) Samples required:

(*a*) If the batch is packaged for repacking or for use in the manufacture of another drug:

(*1*) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

(*2*) For sterility testing: 20 packages, each containing approximately 300 milligrams.

(*b*) If the batch is packaged for dispensing:

(*1*) For all tests except sterility: A minimum of 10 immediate containers, except if each contains less than 450 milligrams, a minimum of 16 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed for ampicillin in § 436.105 of this chapter, using the ampicillin working standard as the standard of comparison and preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.1*M* potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration; and also if it is packaged for dispensing, reconstitute as directed in the labeling. Then, using a suitable hypodermic needle and syringe, remove the withdrawable contents from each container represented as a single-dose container; or if the labeling specifies the amount of potency in a given volume of the resultant preparation, withdraw an accurately measured representative portion from each container. Dilute the sample thus obtained with sufficient solution 3 to give a stock solution of convenient concentration. Further dilute the stock solution with solution 3 to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter using a solution containing the equivalent of 18 milligrams of ampicillin per milliliter.

(4) [Reserved]

(5) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter (or using a solution reconstituted as directed in the labeling, if it is packaged for dispensing).

(7) *Hetacillin content.* Proceed as directed in § 440.25(b)(5), except use about 110 milligrams of sample and calculate the potassium hetacillin content as follows:

$$\text{Percent hetacillin} = \frac{C \times 5{,}000 \times P}{\text{Weight of sample in milligrams}}$$

where:

C=Concentration in milligrams of hetacillin per milliliter of the final solution of the sample obtained from the standard response line.

P=Hetacillin content of the hetacillin working standard in percent.

(8) *Identity.* Proceed as directed in § 436.211 of this chapter, using a 1 percent potassium bromide disc prepared as directed in paragraph (b)(1) of that section.

(9) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[39 FR 19876, May 30, 1974, as amended at 42 FR 59857, Nov. 22, 1977; 43 FR 2393, Jan. 17, 1978; 44 FR 10379, Feb. 20, 1979; 50 FR 19918, May 13, 1985]